Claim Rejection Under 35 U.S.C. § 112

Claims 7-11, 13, 14, 32, and 33 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants have amended the claims to more clearly claim the invention. Applicants have amended "and/or" in Claims 7 and 14 to recite "or". From the two or more oligonucleotides at least one oligonucleotide is homologous to SEQ ID NO: 1 or that at least one nucleotide is homologous to a sequence selected from a group of sequences recited in the claims. These nucleotide sequences may also comprise complements of SEQ ID NO:1 (see for example, page 7, line 32 of the specification).

Claim 33 was amended to recite "reagents", rather than "media", as proposed by the Examiner. Applicants assert that the presently claimed invention is clearly claimed. Applicants respectfully request withdrawal of the rejection on this basis.

Claim Rejection Under 35 U.S.C. § 102

Claims 1, 2, 5, 7-10, 13, 14, 31, and 32 were rejected under 35 U.S.C. § 102(b) as being anticipated by Unal. Unal teaches primers for amplifying the *femA* gene of *Staphylococcus*, including a 23-mer forward primer which is 100% homologous to nucleotides 765-786 of SEQ ID NO:1 and a 19-mer reverse primer which is 95% complementary to nucleotides 1735-1753 of SEQ ID NO:1. Applicants have amended Claims 1, 2, 5 and 7 to recite, *inter alia*, a nucleotide sequence of about 25 to 350, 25 to 250, 25 to 45, and 25 to 45 base pairs of the "consensus" *femA* nucleotide sequence SEQ ID NO:1, respectively. Unal does not disclose a nucleotide sequence of these size ranges with homology to SEQ ID NO:1. Thus Applicants assert that the disclosure of Unal does not anticipate the presently claimed invention.

Furthermore, Applicants note that Claim 13, 14, and 33 relate to a method and a diagnostic kit for identifying various types of *Staphylococci* strains, including coagulase-negative *Staphylococcus*. These methods use oligonucleotides such as probes or primers derived from the consensus sequence for the molecular genotyping of different *Staphylococci* strains. The characterized consensus sequence highlights conserved regions within the *femA* gene of *Staphylococci* strains.

Applicants assert that Unal does not disclose a method for identifying various types of *Staphylococci* strains. Unal describes methods for detecting the use of a specific couple of

primers to target the *femA* gene and to specifically detect *Staphylococci aureus*. However, this strategy does not allow detecting any other *Staphylococcus* species. In particular the reference explicitly states that this specific couple of primers cannot be used to detect coagulase-negative *Staphylococci* by PCR techniques (see the abstract and the "probing section" on page 1688, right column, of Unal). Thus, Applicants assert that the presently claimed invention is not anticipated by Unal. Applicants respectfully request withdrawal of the rejection on this basis.

Claims 1, 2, 5, 7-11, 31, and 32 were rejected under 35 U.S.C. § 102(b) as being anticipated by Alborn et al. Alborn teaches a *Staphylococcus epidermis femA* nucleotide sequence. Applicants have amended Claims 1, 2, 5 and 7 to recite, *inter alia*, a nucleotide sequence of about 25 to 350, 25 to 250, 25 to 45, and 25 to 45 base pairs of the "consensus" *femA* nucleotide sequence SEQ ID NO:1, respectively. Alborn does not disclose a nucleotide sequence of these size ranges with homology to SEQ ID NO:1. Thus Applicants assert that the disclosure of Alborn does not anticipate the presently claimed invention.

Furthermore, Applicants assert that Alborn does not disclose a method for identifying various types of *Staphylococci* strains. Alborn discloses the *femA* gene of *Staphylococcus epidermis* and degenerate sequences thereof, the protein encoded by the *femA* gene, and vectors and microorganisms comprising genes encoding the FemA protein. Alborn refers to the use of a specific couple of primers to target the *femA* gene and to specifically detect *Staphylococcus epidermis*. However, this strategy does not allow detection of any other *Staphylococcus* species. Applicants assert that the presently claimed invention is not anticipated by Alborn. Applicants respectfully request withdrawal of the rejection on this basis.

Claim Rejection Under 35 U.S.C. § 103(a)

Claim 33 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Unal in view of the Stratagene Catalog. Unal relates to the detection of methicillin resistance of *Staphylococci* and not to a diagnostic device for the identification of *Staphylococci* species. The primer sequences provided by Unal only allow specific identification of *Staphylococcus aureus*. Moreover, Unal states that the primer sequences provided do not allow detection of the femA gene in coagulase-negative *Staphylococcus*. (see abstract and page 1688, right column).

Therefore, Applicants assert that it would not be obvious to one of ordinary skill in the art

to identify nucleotide sequences and to use these sequences in methods or kits for identifying various types of known and unknown *Staphylococcus* species based on the primer sequences provided by Unal in combination with the general information on DNA assay kits provided in the Stratagene catalog. Applicants respectfully request withdrawal of the rejection on this basis.

Conclusion

In view of the forgoing remarks and amendments Applicants respectfully request withdrawal of the claim rejections and the objection to the specification. Should any issues arise which may delay prosecution of the present application the Examiner is respectfully requested to contact the undersigned at the telephone number below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Jan. 3, 2003

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Deletions are in **[bold and brackets]** and insertions are underlined.

IN THE SPECIFICATION:

Please amend the paragraph beginning on page 8, line 16 as follows:

Preferably, the oligonucleotide according to the invention is selected from the group consisting of the following nucleotide sequences:

- ANAATGAANTTTACNAATTTNACNGCNANAGANTT (SEQ ID NO: 2) and more particularly *femS1* TAATGAAGTTTACAAAATTT (SEQ ID NO: 3) or femS2 TAATGAAGTTTACNAAATTT (SEQ ID NO: 4)
- ATGNCNNANAGNCATTTNACNCANA (SEQ ID NO: 5) and more particularly *femU1* ("universal" sequence sense of the multiplex PCR): TGCCATATAGTCATTTACGC (SEQ ID NO: 6)
- TAGTNGGNATNAANAANAANNATAANGANGTNATTGC (SEQ ID NO: 7)
- GTNCCNGTNATGAAANTNTTNAANTANTTTTATTC (SEQ ID NO: 8)
- AATGCNGGNNANGATTGG (SEQ ID NO: 9)
- GNAANNGNAANACNAAAAAAGTNNANAANAATGGNGTNAAAGT (SEQ ID NO: 10) and more particularly *fsq1S* (et *1AS*): AAAAAGTTCAAAAAATGG (SEQ ID NO: 11) and *fsq2S* (and *2AS*): AAAAAGTACAAAAAATGG (SEQ ID NO: 12)
- AAGANGANNTNCCNATNTTNNGNTCATTNATGGANGATAC (SEQ ID NO: 13)
- TATATNNANTTTGATGANTA (SEQ ID NO: 14)
- AANGANATNGANAAANGNCCNGANAANAAAAA (SEQ ID NO: 15) and more particularly *fsq3S* (and *3AS*): AAAGATATTGAAAAACGA (SEQ ID NO: 16), *fsq4S* (and *4AS*): AAAGATATTGAAAAGAGACC (SEQ ID NO: 17), *fsq5S* (and *5AS*): AAAGATATCGAGAAAGAC (SEQ ID NO: 18) and *fsq6S* (and *6AS*): AAAGACATCGACAAGCGT (SEQ ID NO: 19)**[.]**
- ANCATGGNAANGAATTACCNAT (SEQ ID NO: 20) and more particularly *fem1* (primer for the production of a probe and of marked amplicons for reverse hybridization experiment): GAACATGGTAATGAATTAC (SEQ ID NO: 21)
- AATCCNTNTGAAGTNGTNTANTANGCNGGTGG (SEQ ID NO: 22)
- AGNTATGCNNTNCAATGGNNNATGATTAANTATGC (SEQ ID NO: 23)

- TTTANNGANGANGCNGAAGATGNNGGNGTNNTNAANTTNAAAAA (SEQ ID NO: 24) and more particularly *fem3bio* (primer for the production of a probe and of marked amplicons for reverse hybridization experiment): GTTGGTGACTTTATTAAACC (SEQ ID NO: 25)
- ATGAAATTTACAGAGTTAA (=*femAS1*) (SEQ ID NO: 26).

Please amend the paragraph beginning on page 10, line 8 as follows:

Advantageously, said "specific primer" is selected from the group consisting of the following nucleotide sequences:

- ACAGCAGATGACATCATT (SEQ ID NO: 29)
- TAATGAAAGAAATGTGCTTA (SEQ ID NO: 30)
- ACACAACTTCAATTAGAAC (SEQ ID NO: 31)
- AGTATTAGCAAATGCGG (SEQ ID NO: 32)
- ATGCATATTTTCCGTAA (SEQ ID NO: 33)
- CAGCAGATGACATCATT (SEQ ID NO: 34)
- CATCTAAAGATATATTAAATGGA (SEQ ID NO: 35)
- AGTATTAGCAAATGCGGGTCAC (SEQ ID NO: 36)
- CAACACAACTTCAATTAGAA (SEQ ID NO: 37).

Please amend the paragraph beginning on page 17, line 25 as follows:

In order to purify bacterial DNA, 200 µl of supernatent were then filtered on a Macherey-Nagel Nucleospin C+T® column and eluted with 200 µl sterile H_2O. Two different amounts of DNA suspension (2 µl and 200 µl) were submitted to multiplex PCR amplification with the primers 5'-TGGCTATCGTGTCACAATCG-3' (SEQ ID NO: 38) and 5'-CTGGAACTTGTTGAGCAGAG-3' (SEQ ID NO: 39) for *mecA* and the above-described primers for *femA*, yielding different fragments.

IN THE CLAIMS:

Please cancel Claims 6, 11, 15-23, 31, 32, and 34-42.

Please amend the following claims:

1. (Twice Amended) An isolated or purified oligonucleotide for the specific identification of *Staphylococci* species, comprising a nucleotide sequence of about 25**[15]** to 350 base pairs of the "consensus" *femA* nucleotide sequence SEQ ID NO:1.

2. (Twice Amended) The oligonucleotide according to claim 1 comprising a nucleotide sequence of about 25**[17]** to 250 base pairs of SEQ ID NO:1.

5. (Twice Amended) The oligonucleotide according to claim 1, wherein the nucleotide sequence comprises about 25**[15]** to 45 base pairs.

7. (Three Times Amended) Two or more isolated or purified oligonucleotides for the specific amplification of *Staphylococci* species comprising at least one nucleotide sequence of about 25**[15]** to 45 base pairs more than 60% homologous to SEQ ID NO:1 **[and/]**or at least one oligonucleotide about 25**[15]** to 45 base pairs more than 60% homologous to SEQ ID NOS:1**[,]** and 29-37**[46, 48, 50, and 52]**.

8. (Twice Amended) The oligonucleotides according to Claim 7 wherein said oligonucleotides have more than 70% homology to SEQ ID NOS:1**[,]** and 29-37**[46, 48, 50, and 52]**.

9. (Twice Amended) The oligonucleotides according to Claim 8 wherein said oligonucleotides have more than 80% homology to SEQ ID NOS:1**[,]** and 29-37**[46,48, 50, and 52]**.

10. (Twice Amended) The oligonucleotides according to Claim 9 wherein said oligonucleotides have more than 90% homology to SEQ ID NOS:1**[,]** and 29-37**[46, 48, 50, and 52]**.

13. (Twice Amended) A method of identification and/or quantification of a *Staphylococci* species, which may present resistance to antibiotics and which is present in a sample, said method comprising the steps of:

obtaining a nucleotide sequence from a *Staphylococci* species present in the sample,

amplifying said nucleotide sequence with two or more isolated oligonucleotides for the specific amplification of *Staphylococci* species comprising at least one nucleotide sequence of about 15 to 45 base pairs more than 60% homologous to SEQ ID NO: 1 or at least one oligonucleotide about 15 to 45 base pairs more than 60%

homolgouse to SEQ ID NOS: 1 and 29-37**[the oligonucleotides according to Claim 7]**, and

identifying and/or quantifying the specific *Staphylococci* species:

by reverse hybridization of the amplified nucleotide sequence with one or more oligonucleotide(s) having a nucleotide sequence comprising about 15 to 350 base pairs of SEQ ID NO:1, specific of said *Staphylococci* species wherein said nucleotide sequence is immobilized on a solid support or

by a comparative measure of the length of the amplified nucleotide sequence.

14. (Twice Amended) A diagnostic device for the identification of *Staphylococci* species comprising: an oligonucleotide having a nucleotide sequence comprising about 15 to 350 base pairs of SEQ ID NO:1, **[and/]**or two or more isolated or purified oligonucleotides for the specific amplification of *Staphylococci* species comprising at least one nucleotide sequence of about 15 to 45 bases pairs more than 60% homologous to SEQ ID NO: 1 or at least one oligonucleotide about 15 to 45 base pairs more than 60% homologous to SEQ ID NOS: 1 and 29-37**[the two or more oligonucleotides according to Claim 7]**.

33. (Amended) The diagnostic device of Claim 14 further comprising reagents**[all of the media]** necessary for the identification of an amplified sequence of said *Staphylococci* species through any one of the methods selected from the group consisting of: *in situ* hybridization, hybridization on a solid support, hybridization in solution, hybridization on a dot blot, Northern blot, Southern blot, probe hybridization by the use of an isotopic label, probe hybridization by the use of a non-isotopic label, genetic amplification and a mixture thereof.

Please add the following claims:

43. (NEW) A method according to claim 13 wherein said oligonucleotides have more than 70% homology to SEQ ID NOS: 1, 46, 48, 50, and 52.

44. (NEW) A method according to claim 13 wherein said oligonucleotides have more than 80% homology to SEQ ID NOS: 1, 46, 48, 50, and 52.

45. (NEW) A method according to claim 13 wherein said oligonucleotides have more than 90% homology to SEQ ID NOS: 1, 46, 48, 50, and 52.

46. (NEW) A method according to claim 13 wherein said oligonucleotides are selected from the group consisting of SEQ ID NOS: 1, 18-40, 42, and 44.

47. (NEW)A diagnostic kit according to claim 14 wherein said oligonucleotides have more than 70% homology to SEQ ID NOS: 1, 46, 48, 50, and 52.

48. (NEW)A diagnostic kit according to claim 14 wherein said oligonucleotides have more than 80% homology to SEQ ID NOS: 1, 46, 48, 50, and 52.

49. (NEW)A diagnostic kit according to claim 14 wherein said oligonucleotides have more than 90% homology to SEQ ID NOS: 1, 46, 48, 50, and 52.

50. (NEW) A diagnostic kit according to claim 14 wherein said oligonucleotides are selected from the group consisting of SEQ ID NOS: 1, 18-40, 42, and 44.